<table>
<thead>
<tr>
<th>AREA OF FOCUS</th>
<th>WHAT DOES IT MEAN?</th>
<th>WHERE SHOULD IT BE INCLUDED IN THE APPLICATION?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scientific Premise</td>
<td>The <strong>scientific premise</strong> for an application is the research that is used to form the basis for the proposed research question(s). Describe the general strengths and weaknesses of the prior research being cited as crucial to support the application. Consider discussing the rigor of previous experimental designs, as well as the incorporation of relevant biological variables and authentication of key resources. <em>See related FAQs, blog post</em>*</td>
<td>Research Strategy ➢ Significance **</td>
</tr>
<tr>
<td>Scientific Rigor (Design)</td>
<td>Scientific rigour is the strict application of the scientific method to ensure robust and unbiased experimental design, methodology, analysis, interpretation and reporting of results. Emphasize how the experimental design and methods proposed will achieve robust and unbiased results. <em>See related FAQs, blog post, examples from pilots</em>*</td>
<td>Research Strategy ➢ Approach **</td>
</tr>
<tr>
<td>Biological Variables</td>
<td>Biological variables, such as sex, age, weight, and underlying health conditions, are often critical factors affecting health or disease. In particular, sex is a biological variable that is frequently ignored in animal study designs and analyses, leading to an incomplete understanding of potential sex-based differences in basic biological function, disease processes and treatment response. Explain how relevant biological variables, such as the ones noted above, are factored into research designs, analyses, and reporting in vertebrate animal and human studies. Strong justification from the scientific literature, preliminary data or other relevant considerations must be provided for applications proposing to study only one sex. <em>See related FAQs, blog post, article</em>*</td>
<td>Research Strategy ➢ Approach **</td>
</tr>
<tr>
<td>Authentication</td>
<td>Key biological and/or chemical resources include, but are not limited to, cell lines, specialty chemicals, antibodies and other biologics. Briefly describe methods to ensure the identity and validity of key biological and/or chemical resources used in the proposed studies. These resources may or may not be generated with NIH funds and: • may differ from laboratory to laboratory or over time; • may have qualities and/or qualifications that could influence the research data; • are integral to the proposed research. The authentication plan should state in one page or less how you will authenticate key resources, including the frequency, as needed for your research. Note: Do not include authentication data in your plan. <em>See related FAQs, blog post</em>*</td>
<td>Other Research Plan Section ➢ Include as an attachment ➢ Do not include in the Research Strategy. **</td>
</tr>
</tbody>
</table>

**This chart is based on general instructions for research grant and mentored career development applications. It should only be used as a guide. For all applications, please read the applicable Funding Opportunity Announcement (FOA) & Application Guide for specific instructions.**
New NIH requirement: Rigor and Reproducibility in Grant Applications

- Applies to research grants and mentored career development awards
- Updates to institutional training grants, institutional career development awards (K12/KL2) and individual fellowships will be forthcoming in 2017 or later.

The updates to NIH research grant and career development award application instructions and review language focus on four key areas:

1. **The scientific premise of the proposed research**
   - The scientific premise for an application is the research that is used to form the basis for the proposed research question(s). NIH expects applicants to describe the general strengths and weaknesses of the prior research being cited by the applicant as crucial to support the application. It is expected that this consideration of general strengths and weaknesses could include attention to the rigor of the previous experimental designs, as well as the incorporation of relevant biological variables and authentication of key resources.

   **KEY TAKE AWAY:** establish the niche of your research, show gaps/shortcomings in previous research, show how you can extend previous research (including yours)

2. **Rigorous experimental design for robust and unbiased results**
   - Scientific rigor is the strict application of the scientific method to ensure robust and unbiased experimental design, methodology, analysis, interpretation and reporting of results. This includes full transparency in reporting experimental details so that others may reproduce and extend the findings.

   **KEY TAKE AWAY:** Detail your methodology and research design. Other researchers should be able to replicate your study based on your description

3. **Consideration of relevant biological variables**
   - Biological variables, such as sex, age, weight, and underlying health conditions, are often critical factors affecting health or disease. In particular, sex is a biological variable that is frequently ignored in animal study designs and analyses, leading to an incomplete understanding of potential sex-based differences in basic biological function, disease processes and treatment response.
   - NIH expects that sex as a biological variable will be factored into research designs, analyses, and reporting in vertebrate animal and human studies. Strong justification from the scientific literature, preliminary data or other relevant considerations must be provided for applications proposing to study only one sex.

   **KEY TAKE AWAY:** Account for sex as a biological variable, justify reasons if not

4. **Authentication of key biological and/or chemical resources**
   - Key biological and/or chemical resources include, but are not limited to, cell lines, specialty chemicals, antibodies and other biologics. Key biological and/or chemical resources may or may not be generated with NIH funds and:
     1. may differ from laboratory to laboratory or over time;
may have qualities and/or qualifications that could influence the research data;
3. are integral to the proposed research.

- The quality of resources used to conduct research is critical to the ability to reproduce the results. Each investigator will have to determine which resources used in their research fit these criteria and are therefore key to the proposed research.

**KEY TAKE AWAY:** New attachment, needed only if key biological and/or chemical resources (other than standard) will be used

<table>
<thead>
<tr>
<th>Key Area</th>
<th>Application Instructions</th>
</tr>
</thead>
</table>
| Scientific premise                                 | • In Research Strategy
• Scored under “Significance” criterion          |
| Scientific rigor                                   | • In Research Strategy
• Scored under “Approach” criterion              |
| Consideration of relevant biological variables    | • In Research Strategy
• Scored under “Approach” criterion              |
| Authentication of key biological and/or chemical resources | • New attachment
• Not scored                                      |

**Scored Review Criteria**

<table>
<thead>
<tr>
<th>Significance</th>
<th>• Is there a strong scientific premise for the project?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approach</strong></td>
<td>• Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed?</td>
</tr>
<tr>
<td></td>
<td>• Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?</td>
</tr>
<tr>
<td><strong>Additional Review Considerations</strong></td>
<td>• For projects involving key biological and/or chemical resources, reviewers will comment on the brief plans proposed for identifying and ensuring the validity of those resources.</td>
</tr>
<tr>
<td><strong>Authentication of Key Biological and/or Chemical Resources</strong></td>
<td></td>
</tr>
</tbody>
</table>

**If in doubt and for questions:**
Email: reproducbility@nih.gov

**NIH Guidance, FAQs, and Open Mike blog post:**

- [https://grants.nih.gov/reproducibility/index.htm#guidance](https://grants.nih.gov/reproducibility/index.htm#guidance)
- [http://grants.nih.gov/reproducibility/faqs.htm#IV](http://grants.nih.gov/reproducibility/faqs.htm#IV)
• Describe methods to ensure the identity and validity of key biological and/or chemical resources (may include cell lines, specialty chemicals, antibodies, other biologics).

• Do not put preliminary data and other methods in this section

• You do not need to provide authentication data itself in this one page attachment; reviewers will be asked to assess the adequacy of the plans you propose for authenticating key resources.

• Purchased or established resources may have been authenticated prior to receipt, and the vendor may have included a specification sheet with the product. If the authentication data provided by the vendor meets your needs in terms of how the product will be used, this may be mentioned this in the plan, but you should also include a plan to independently verify the identity and activity of the product before use. If the product will be used long-term, consider the stability of the product and how the validity of the product will be assessed over time.

• Key resources developed in-house should also be regularly authenticated and plans to do so should be provided in this section.

• **Standard laboratory reagents that are not expected to vary do not need to be included in the plan. Examples are buffers and other common biologicals or chemicals.**

**Tips**

**Chemicals**
Chemicals purchased commercially come with an authentication sheet identifying the purity and contaminant.

**Cell lines**
Human cell lines acquired from ATCC (American Type Tissue Collection, a major provider of cell lines to research scientists) and other commercial cell line providers assess all of their lots of their cell lines by Short Tandem Repeats, which allows one to distinguish one DNA sample from another and allows the unique identification of specific cell lines. The non-human lines have interspecies analysis performed on each lot of cell lines. All of this information is readily available to their customers on the company’s website.

**Primary cell lines**
Primary cell lines that are isolated in individual labs or from commercial facilities are identified by surface markers which are unique to each isolated primary cell line. These markers are identified by flow cytometry or by immunohistochemistry, which are techniques with high sensitivity to accurately identify expression markers that identify specific cells.

**Antibody specificity**
The specificity for individual antibodies are identified by western blot analysis, where antibodies to specific antigens can be visualized on an electrophoresis gel.
Suggested template

All key resources for this proposal will be authenticated to enhance the reproducibility of our results, as appropriate and according to NIH policy.

Key biological resources that will be utilized in this proposal include:

1. Cell lines: xxxx
2. Transgenic mouse strains: xxxxx
3. Antibodies: xxxxx
4. Etc

• Cell lines will be validated via...<describe methods, including short tandem repeat (STR) analysis if appropriate>
• Transgenic mouse strains are validated by...<describe techniques for genotyping, etc>
• Antibodies will be confirmed by...<describe methods>

All other antibodies and reagents we anticipate using for the proposed work are commercially available and validated by the companies that provide them. Other resources used in this proposal will be standard laboratory reagents. Should we need to generate or obtain additional unique resources in the course of this proposal, they will be authenticated using methods similar to those described above, as appropriate.

NOTE: Do not include preliminary data

Sources: https://ctsi.ucla.edu/funding/files/view/docs/2016_NIH_Requirements_GrantProposals_UColrado.pdf
https://medicine.umich.edu/medschool/sites/medicine.umich.edu.medschool/files/res_oor_NIH_Authe ntication%20of%20Key%20Biological%20and%20Chemical%20Resources.pdf
Rigor and Reproducibility Checklist

Scientific premise

- Have you discussed the general strengths and weaknesses of the previous experimental designs? These could include attention to the rigor of the previous experimental designs, as well as the incorporation of relevant biological variables and authentication of key resources.

Rigorous experimental design

- Have you detailed your methodology and research design with full transparency?

Consideration of relevant biological variables

- Have you factored sex as a biological variable into research designs, analyses, and reporting?
- If not, have you provided strong justification from the scientific literature, preliminary data or other relevant considerations as to why you will study only one sex?

Authentication of key biological and/or chemical resources

- Will you be using any biological or chemical resources (other than standard) that:
  1. may differ from laboratory to laboratory or over time?
  2. may have qualities and/or qualifications that could influence the research data?
  3. are integral to the proposed research?

- If yes to any of the above, please include details on how you will authenticate/validate them, in a separate attachment (See attached template)

For any questions, please contact pedsra@columbia.edu